PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 042664woMemh	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/011719	International filing date *(day/month/year)* 18.10.2004	Priority date *(day/month/year)* 16.10.2003

International Patent Classification (IPC) or national classification and IPC
C07K7/50, A61K38/12, C07K16/00

Applicant
APLAGEN GMBH et al.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 16 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15.08.2005	24.11.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Weikl, M Telephone No. +49 89 2399-7518

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/011719

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-25	as originally filed
Claims, Numbers	
1-35	filed with telefax on 29.09.2005
Drawings, Sheets	
1/4-4/4	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-25,27-35
	No:	Claims	26
Inventive step (IS)	Yes:	Claims	1-25, 27, 28, 30, 32, 33, 35
	No:	Claims	29, 31, 34
Industrial applicability (IA)	Yes:	Claims	1-36
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Documents

The following documents (D) are referred to in this communication; the numbering corresponds to the order in the International Search Report:

D1: US 2002/151473 A1 (BRAISTED ANDREW C ET AL) 17 October 2002 (2002-10-17)

D2: PHELAN J C ET AL: 'A general method for constraining short peptides to an [alpha]-helical conformation' JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 1997 UNITED STATES, vol. 119, no. 3, 1997, pages 455-460, XP002267339 ISSN: 0002-7863

D3: JACKSON D Y ET AL: 'GENERAL APPROACH TO THE SYNTHESIS OF SHORT ALPHA-HELICAL PEPTIDES' JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 113, no. 24, 1991, pages 9391-9392, XP001157324 ISSN: 0002-7863

D4: YU C ET AL: 'Synthesis and study of peptides with semirigid i and i + 7 side-chain bridges designed for alpha-helix stabilization.' BIOORGANIC & MEDICINAL CHEMISTRY. ENGLAND JAN 1999, vol. 7, no. 1, January 1999 (1999-01), pages 161-175, XP001157321 ISSN: 0968-0896

D5: TAYLOR JOHN W: 'The synthesis and study of side-chain lactam-bridged peptides' BIOPOLYMERS, vol. 66, no. 1, 2002, pages 49-75, XP002267340 ISSN: 0006-3525

D6: RAUK A ET AL: "Glutathione radical: Intramolecular H abstraction by the thiyl radical" CANADIAN JOURNAL OF CHEMISTRY 2001 CANADA, vol. 79, no. 4, 2001, pages 405-417, XP009046071 ISSN: 0008-4042

D7: HUFFMAN G W ET AL: "SUBSTRATE SPECIFICITY OF ISOPENICILLIN N SYNTHASE" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 35, no. 10, 15 May 1992 (1992-05-15), pages 1897-1914, XP002029802 ISSN: 0022-2623

Subject-matter of the application

The present application relates to the introduction of conformational constraints into short peptides in order to promote an α-helical conformation. For this purpose

applicant proposes to covalently link the side chains at positions *i* and *i+7* (corresponding to two helical turns) of the peptide via a bridge structure. The closed bridge structure is specified to comprise at least one amide and one disulfide bond. In addition, the structure can be stabilized by hydrogen bonds between the peptidic chain and the bridge structure.

Re Item IV.

The claimed subject-matter lacks unity. The separate inventions/groups of inventions are:

Claims 1-28, 30, 32, 33 and 35:

Claims relating to peptidic compounds with covalently closed bridged structures to stabilize an alpha-helical conformation; method of making them; use of building blocks to make them

Claims 29, 31 and 34:

Claims relating to building blocks for the bridge structure with one (claim 31) or two amide bonds (claim 29); method of making them (claim 34)

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

Article 3(4)(iii) in combination with Rule 13.1 PCT stipulates that the international application shall relate to one invention only or to a group so linked as to form a single general inventive concept. Rule 13.2 PCT stipulates that where a group of inventions is claimed in one and the same international application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding 'special technical features', i.e. technical features that define a novel and inventive contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

No such common concept (technical relationship) linking the above groups of inventions could be found. The groups as set out above relate to separate classes of chemical compounds which are BOTH structurally AND functionally different.

Although claims 29, 31 and 34 relate to intermediates of the final products of claims 1-28, 30, 32, 33 and 35, their subject-matter does not fulfil the requirements of section 10.18 of the PCT Guidelines. In particular, none of the compounds of claims 29, 31 and 34 comprises a disulfide bridge which must be seen as an essential structural element of the final product.

In view of the fact that no additional effort was necessary for the international preliminary examination of both groups of inventions, this authority chose NOT to invite the applicant to pay additional examination fees. However, the non-unity objection may become relevant when the present application proceeds to the regional phase.

N.B: It must be pointed out that in principle the second group of inventions could be further subdivided into **at least** two groups, namely building blocks for bridge structures with one amide bond (claims 31 and 34) and two amide bonds (claims 29 and 34). This subdivision can be made since compounds belonging to each of the two compound classes have been described before (Huffman et al., J. Med. Chem. 1992, 35, 1897-1914; Rauk et al., Can. J. Chem. 2001, 79, 405-417; both cited in the International Search Report). Again, this objection may become relevant when the present application proceeds to the regional phase.

INVENTION 1 (claims 1-28, 30, 32, 33 and 35)

Re Item V.

Novelty (Article 33(2) PCT)

Claim 26 relates to *any* antibody which binds to the compounds of the preceding claims. Given the fact that according to claim 26 the claimed antibodies do not necessarily have to bind to the bridge structure, many antibodies which are state of the art will fall within the scope of claim 26. Thus, the subject-matter of claim 26 is not novel in the sense of Article 33(2) PCT.

Re Item VII.

Sufficiency of Disclosure (Article 5 PCT)

1. Claim 1 relates to cyclic bridge structures wherein the bridge connecting two side chains has a variable amount of bridge backbone atoms (ranging from 11 to 17). However, all the examples are restricted to bridge structures with 13 backbone atoms.
The cited prior art indicates that the correct choice of linker length for a given distance is crucial for the stability and native conformation of the helical structures. E.g. document D2 reports that for the purpose of *i* to *i+7 glutamine* tethers, a 4 methylene bridge seems to be optimal. It was calculated that even slight length alterations would involve unfavourable effects on the helical conformation (D2: paragraph bridging pages 456 and 457). Thus, claims wherein the length of the linker/bridge differs from 13 backbone atoms can not be regarded as sufficiently supported by the present application.

Re Item VIII.

Clarity (Article 6 PCT)

1. Current claim 1 relates to the connecting of **at least** two amino acid side chains by a bridge structure. The use of the expression 'at least' creates unclarity since it suggests that more than two side chains could be connected by one bridge

2. Current claim 3 is unclear in that it does not specify that the stabilizing amino acids of the peptide backbone are located between the two branching points.

3. Current claim 11 relates to a peptide having a particular sequence (TKKTQLQL.....). However, the non-exclusive examples given in the same claim sometimes differ from that sequence (especially at the branching points).The same is true for claims 16 and 21 (the latter also does not specify that X stands for homocysteine).

INVENTION 2 (claims 29, 31 and 34):

Re Item V.

Inventive Step (Article 33(3) PCT)

1. Document D6 discloses a compound which can be described by formula (8a) (namely compound 2 of Figure 3). Similarly, document D7 discloses a compound which can be described by formula (7a) (namely compound 45 of Table IV).

   The compounds of current claims 29 and 31 only differ from the compounds of formulas (7a) and (8a) by a rearrangement of the C=O/N-H groups of the amide bonds. No particular technical effect associated with that rearrangement which would account for an inventive activity can be recognized by this authority. Therefore, claims 29 and 31 do not fulfil the requirements of Article 33(3) PCT

2. With the compounds of claims 29 and 31 lacking inventive step, no inventive step can be acknowledged for a method of making them (claim 34).

Claims

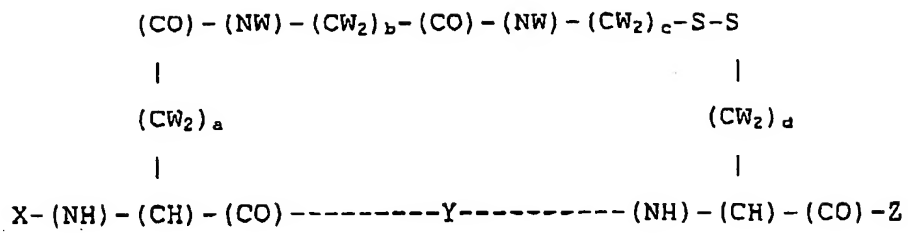
1. Peptidic compounds having covalently closed bridge structures, which branch off from suitable amino acid side chains of a peptide with alpha-helical conformation and which connect at least two amino acid side chains of this peptide which are located at positions i and i+ 7 of the amino acid sequence of the peptide, thereby stabilizing the bridged part of the helix, wherein the bridge backbone, including the side chain atoms of amino acids i and i + 7 of the peptide, consists of one or two amide (peptide) bonds, one disulfide bridge and further 7 to 11, preferably 9 C- or N-atoms.

2. Peptidic compounds according to claim 1, wherein the bridge backbone comprises two amide (peptide) bonds, one sulfide bridge and further 7 carbon atoms.

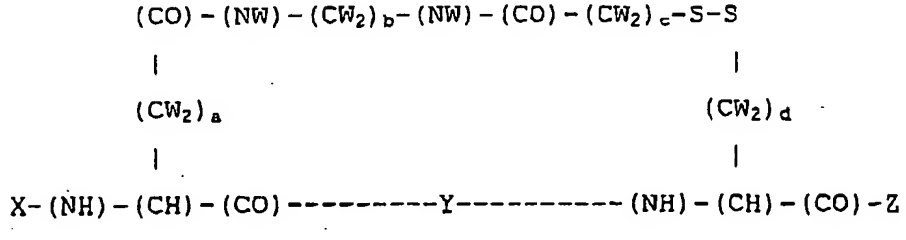
3. Peptidic compounds according to claims 1 and/or 2, wherein the bridge is stabilized by hydrogen bonds between one or more amino acid side chain(s) of the peptide and the bridge, and the stabilizing amino acid(s) is/are selected from lysine, arginine, asparagine, glutamine, aspartic acid, glutamic acid, serine, threonine, thyrosine or histidine and is/are located at position(s) i + 3 and/or i + 4 of the peptides.

4. Peptidic compounds according to claim 3, wherein the stabilizing amino acid(s) is/are aspartate at position i + 3, and/or lysine or glutamine at position i + 4.

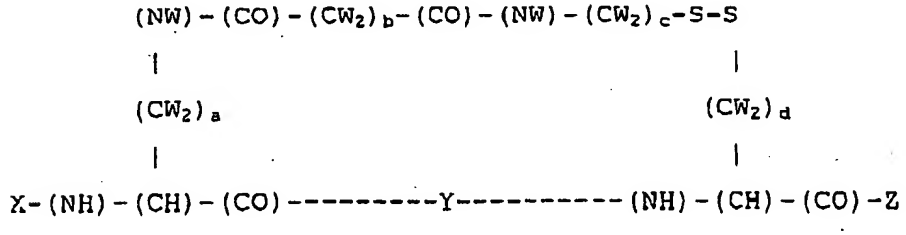
5. Peptidic compounds according to claims 1-4, and represented by the molecules covered by one of the formulas (1a) – (1d):



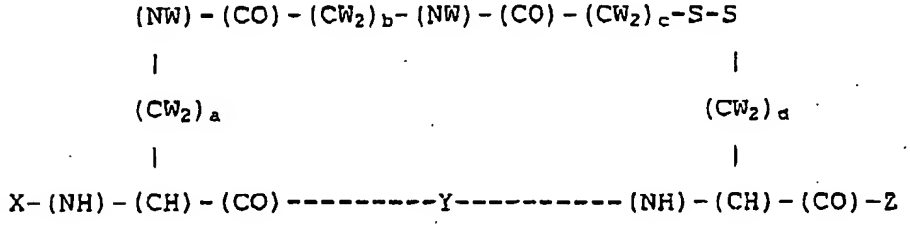
(1a)



(1b)



(1c)

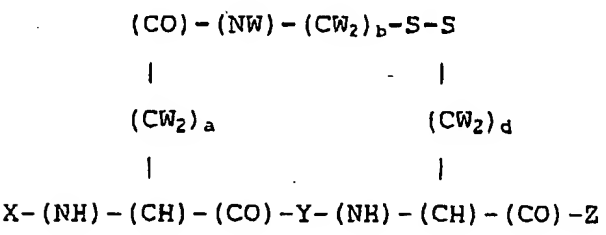


(1d)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1), (2) or (3); a, b, c and d are

independently selected from the integers 1 to 3, provided that the sum a+b+c+d is 7, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

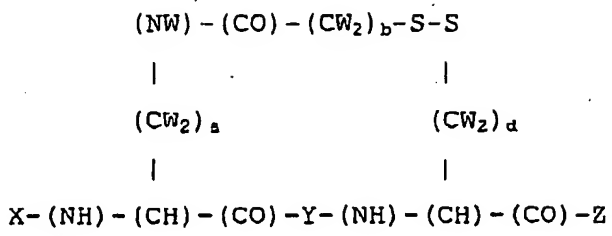
6. Peptidic compounds according to claim 1-4, and represented by the molecules covered by the generic formula (2):



(2)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9; at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

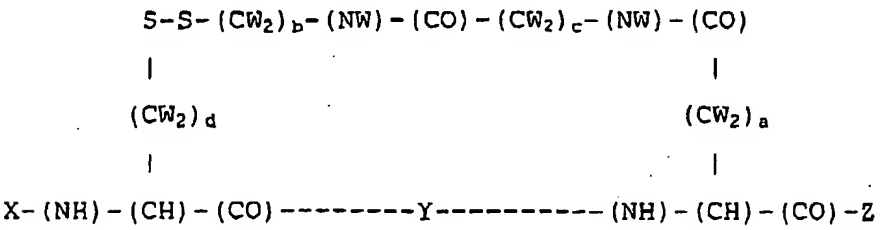
7. Peptidic compounds according to claim 1-4, and represented by the molecules covered by the generic formula (3):



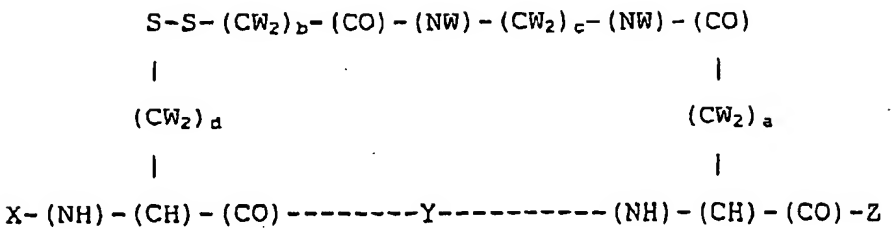
(3)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

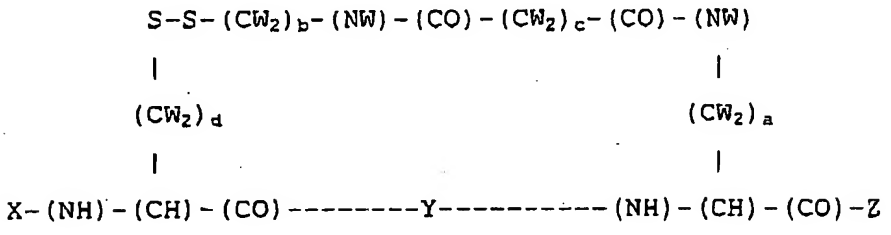
8. Peptidic compounds according to claim 1-4, and represented by the molecules covered by one of the formulas (4a) – (4d):



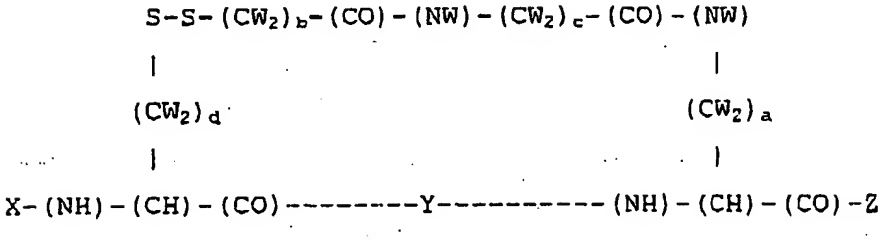
(4a)



(4b)



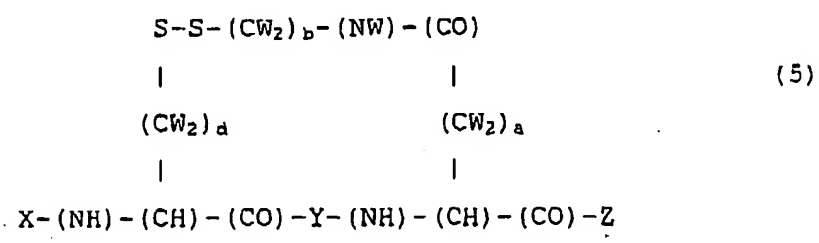
(4c)



(4d)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1) to (2), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1) to (6), a, b, c and d are independently selected from the integers 1 to 3, provided that a+b+c+d is 7, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

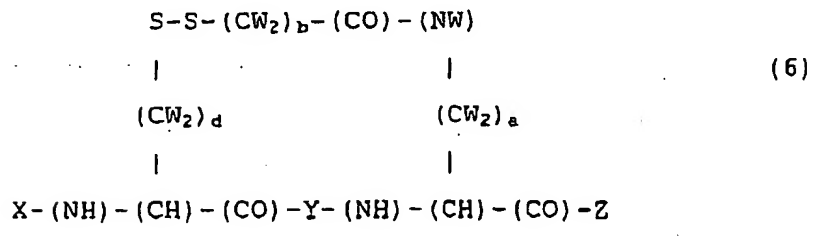
9. Peptidic compounds according to claim 1-4, and represented by the molecules covered by the generic formula (5):



(5)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1) to (6), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1) to (6), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9, W is hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl molety with at least one hydroxyl-, carboxyl- or amino group, a peptide of maximally 30 amino acids, a polyethyleneglycol moiety, or a naturally occurring or artifical sugar molecule and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

10. Peptidic compounds according to claim 1-4, and represented by the molecules covered by the generic formula (6):

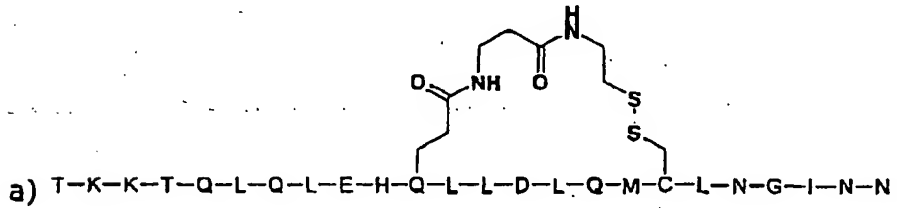


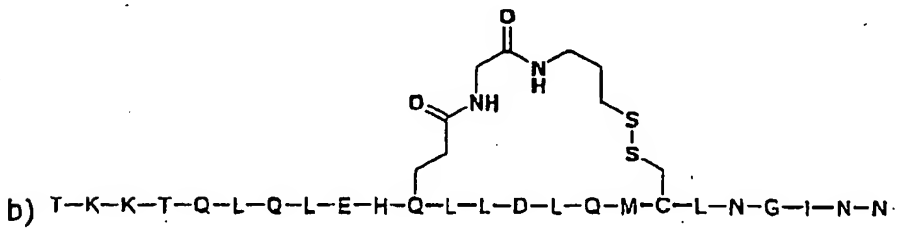
(6)

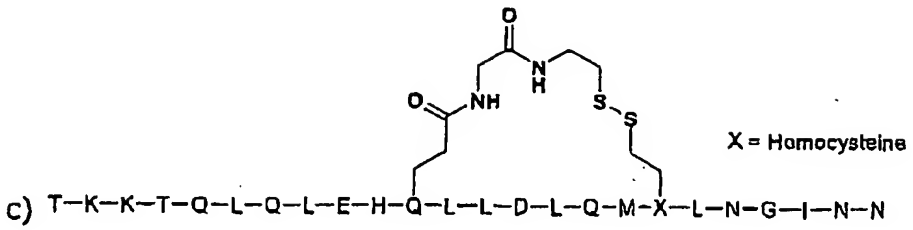
wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1) to (6), Y is any amino acid sequence consisting

of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1) to (6), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

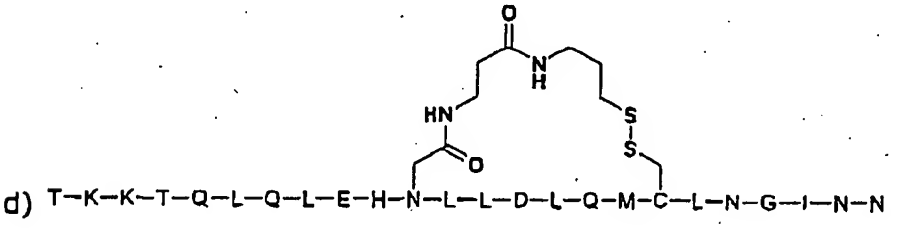
11. Peptidic compounds according to claims 1-10, binding to the interleukin 2 receptor and containing the stabilized peptide sequence TKKTQLQLEHKLLDLQMXLNGINN in a helical conformation, where X stands for homocysteine and two helical turns are bridged by a backbone according to claims 1-10; thereby including non-exclusively the sequences and structures (a- f) as follows:



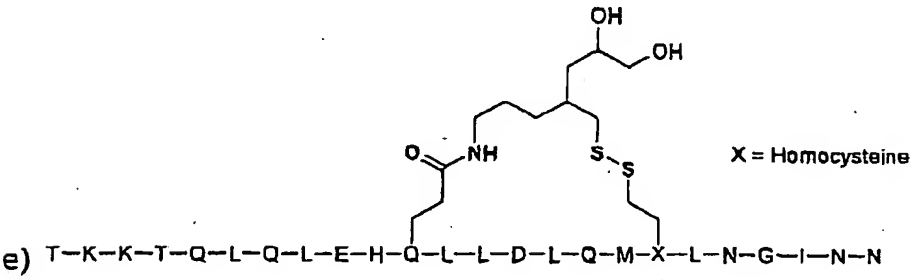




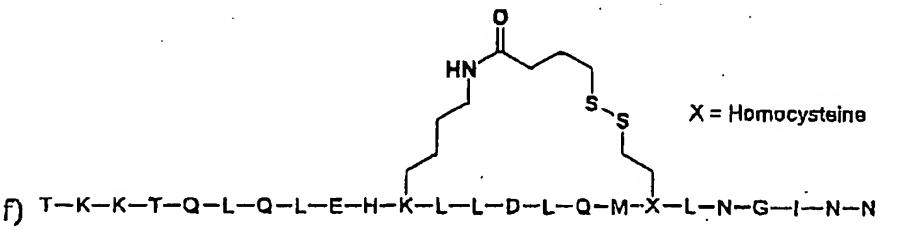
c) T–K–K–T–Q–L–Q–L–E–H–Q–L–L–D–L–Q–M–X–L–N–G–I–N–N



d) T–K–K–T–Q–L–Q–L–E–H–N–L–L–D–L–Q–M–C–L–N–G–I–N–N



e) T–K–K–T–Q–L–Q–L–E–H–Q–L–L–D–L–Q–M–X–L–N–G–I–N–N



f) T–K–K–T–Q–L–Q–L–E–H–K–L–L–D–L–Q–M–X–L–N–G–I–N–N

12. Peptidic compounds according to claim 11, in which the bridging structure is shifted along the peptide sequence in such a way that binding to the interleukin 2 receptor is maintained and another part of the overall helical structure is bridged by the construct.

13. Peptidic compounds according to claims 11 and 12, in which at least one amino acid of the peptide sequence is replaced by physicochemically

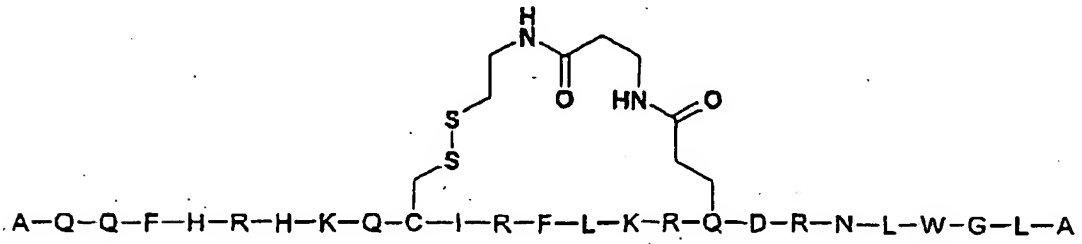
related natural or non-natural amino acids in a conservative exchange, which maintains the binding of the peptide to the Interleukin 2 Receptor.

14. Peptidic compounds according to claims 11-13, which are N- and/or C-terminally modified in such a way that the binding of the peptide to the Interleukin 2 receptor is maintained and/or water solubility is improved and/or that exopeptidases can not cleave at the terminal sites, whereby terminal modifications include non-natural amino acids, D-amino acids, sugar moieties or freely chosen appropriate organic moieties.

15. Pharmaceutical preparations containing an active ingredient according to claims 11-14 and intended for use in humans or animals as an antagonist of the action of the cytokine Interleukin 2.

16. Peptidic compounds according to claims 1-10, binding to the interleukin 4 receptor and containing the stabilised peptide sequence AQQFHRHQCIRFLKRQDRNLWGLA in a helical conformation, wherein two helical turns are bridged by a backbone according to claims 1-10, thereby including non-exclusively the following sequence and structure (g):

g)



17. Peptidic compounds according to claim 16, in which the bridging structure is shifted along the peptide sequence in such a way that binding to the interleukin 4 receptor is maintained and another part of the overall helical structure is bridged by the construct.

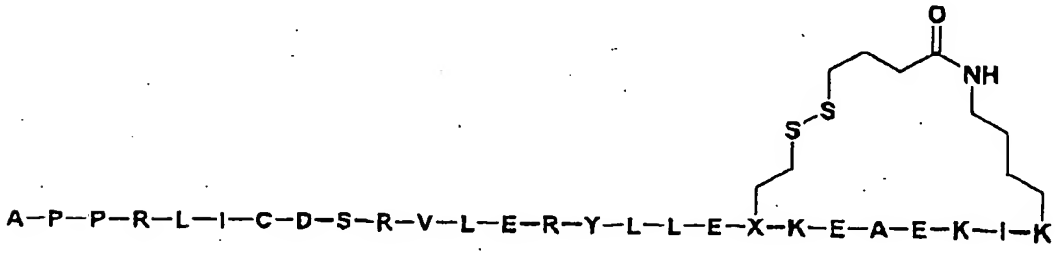
18. Peptidic compounds according to claims 15-16, in which at least one amino acid of the peptide sequence is replaced by physicochemically related natural or non-natural amino acids in a conservative exchange, which maintains the binding of the peptide to the Interleukin 4 receptor.

19. Peptidic compounds according to claims 16-18, which are N- and/or C-terminally modified in such a way that the binding of the peptide to the Interleukin 4 receptor is maintained and/or water solubility is improved and/or that exopeptidases can not cleave at the terminal sites, whereby terminal modifications include non-natural amino acids, D-amino acids, sugar moieties or freely chosen appropriate organic moieties.

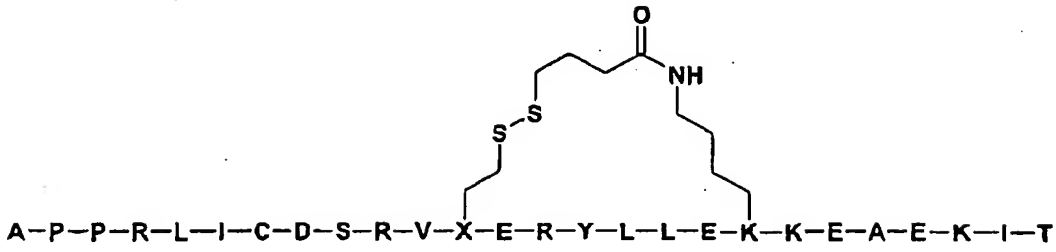
20. Pharmaceutical preparations containing an active ingredient according to claims 16-18 and intended for use in humans or animals as an antagonist of the action of the cytokine Interleukin 4.

21. Peptidic compounds according to claims 1-19, binding to the erythropoietin receptor and containing the stabilised peptide sequence APPRLICDSRVLERYLLEXKEAEKIK in a helical conformation, wherein two helical turns are bridged by a backbone according to claims 1-13; thereby including non-exclusively the following sequences and structures (h-l):

h)



i)



22. Peptidic compounds according to Claim 21, in which the bridging structure is shifted along the peptide sequence in such a way that binding to the erythropoietin receptor is maintained and another part of the overall helical structure is bridged by the construct.

23. Peptidic compounds according to claims 21-22, in which at least one amino acid of the peptide sequence is replaced by physicochemically related natural or non-natural amino acids in a conservative exchange, which maintains the binding of the peptide to the erythropoietin receptor.

24. Peptidic compounds according to claims 21-23, which are N- and/or C-terminally modified in such a way that the binding of the peptide to the erythropoietin receptor is maintained and/or water solubility is improved and/or that exopeptidases can not cleave at the terminal sites, whereby terminal modifications include non-natural amino acids, D-amino acids, sugar moieties or freely chosen appropriate organic moieties.

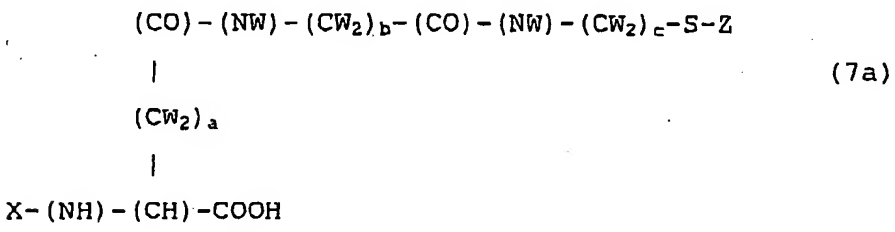
25. Pharmaceutical preparations containing an active ingredient according to claims 16-19 and intended for use in humans or animals as an agonist of the action of the cytokine erythropoietin.

26. Mono- and polyclonal antibodies to the substances covered by Claims 1-25, and the use of such antibodies in diagnostic and pharmacological

quantification and/ or inhibition of action of the active substances in body fluids or tissues of animals or humans.

27. Peptidic compounds according to claims 1-14, 16-19 and/or 21-24, in which the N-terminal amino acid is acetylated and/or the C-terminal amino acid is amidated.

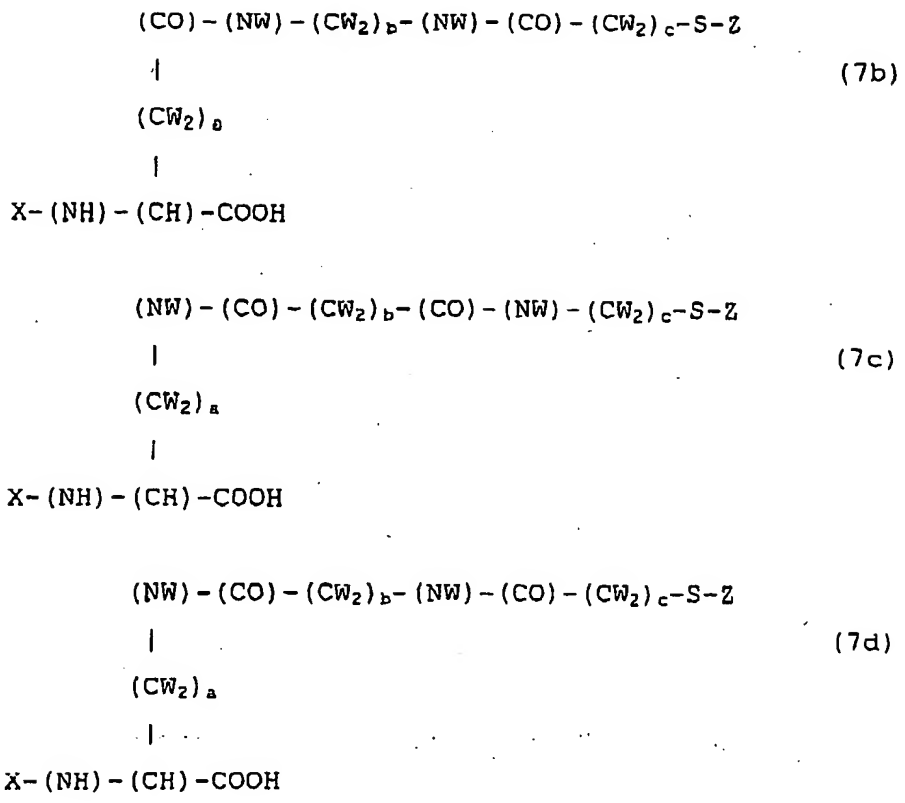
28. Use of a compound according to the generic formula (7a):



(7a)

as building block for the synthesis of peptidic compounds of any of claims 1-14, 16-19 and/or 21-24, wherein X or Z are hydrogen or any protecting group; a, b, and c are independently selected from the integers 1 to 3, provided that the sum a+b+c is an integer from 3 to 6, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule.

29. Compounds as building blocks for the synthesis of peptidic compounds of any of claims 1-14, 16-19 and/or 21-24, represented by the molecules covered by the generic formulas (7b) to (7d):



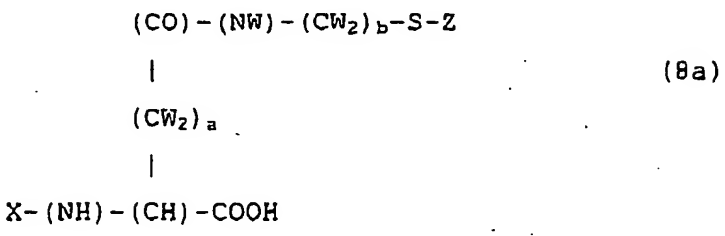
(7b)

(7c)

(7d)

wherein X and Z are hydrogen or any protecting group; a, b, and c are independently selected from the integers 1 to 3, provided that the sum a+b+c is an integer from 3 to 6, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule.

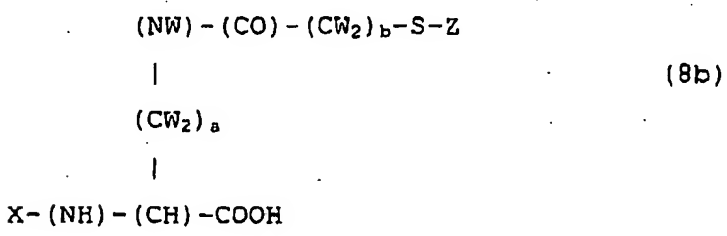
30. Use of a compound according to formula (8a):



(8a)

as building block for the synthesis of peptidic compounds of any of claims 1-14, 16-19 and/or 21-24, wherein X and Z are hydrogen or any protecting group; a and b are independently selected from the integers 1 to 5, provided that the sum a+b is an integer from 2 to 8, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule.

31. Compounds as building blocks for the synthesis of peptidic compounds of any of claims 1-14, 16-19 and/or 21-24, represented by the formula (8b):

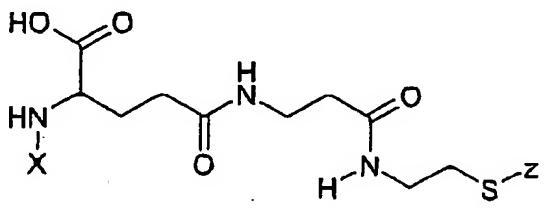


(8b)

wherein X and Z are hydrogen or any protecting group; a and b are independently selected from the integers 1 to 5, provided that the sum a+b is an integer from 2 to 8, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety

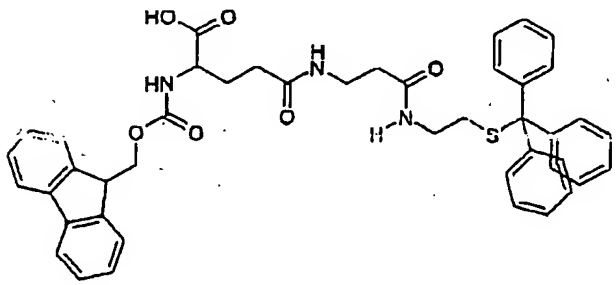
with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule.

32. Use according to claim 28 of the formula (9), wherein X and Z are hydrogen or any protecting group:



(9)

33. Use according to claim 32 of the formula (10):



(10)

34. Methods for synthesis of building blocks according to claims 29 and 31 via solid phase synthesis.

35. Methods for synthesis of peptidic compounds according to claims 1-14, 16-19 and/or 21-24 comprising the following steps:

a. Synthesizing an intermediate peptidic compound by means of peptide synthesis from C- to N-term, comprising introduction of an amino acid containing a protected SH function in its side chain at

position *i+7* (i.e. introduction after deprotection of the N-term of the amino acid at position *i+8*), followed by the introduction of six amino acids at positions *i+6* to *i+1*, and furthermore followed by introduction of a building block according to claims 31-34 at position *i* (i.e. after deprotection of the N-term of the amino acid at position *i+1*) of the growing peptide chain,

b. continuation of the peptide synthesis until the N-terminal amino acid was introduced,

c. removal of the remaining protecting groups,

d. establishing helix-stabilizing conditions, for example with appropriate fluorinated solvents,

e. obtaining the peptidic compound by closure of a disulfide bridge with appropriate reagents under these helix-stabilizing conditions.